ORIGINAL ARTICLE

Neurobehavioural effects among workers occupationally exposed to organophosphorous pesticides

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Aims: To identify neurobehavioural deficits among workers exposed to organophosphorous (OP) pesticides in their occupation.

Methods: This study was conducted during the period when pesticides were applied to cotton crops in the fields in Menoufiya Governorate, Egypt. Fifty two occupationally exposed male workers were compared to 50 unexposed male controls who were similar in age, socioeconomic class, and years of education (⩾12 years). All participants completed a questionnaire (assessing personal, occupational, and medical histories), general and neurological clinical examination, neurobehavioural test battery (including tests for verbal abstraction, problem solving, attention, memory, and visuomotor speed), personality assessment, and serological analysis for serum acetylcholinesterase.

Results: After correcting for confounders of age and education, the exposed participants exhibited significantly lower performance than controls on six neurobehavioural tests (Similarities, Digit Symbol, Trailmaking part A and B, Letter Cancellation, Digit Span, and Benton Visual Retention). A longer duration of work with pesticides was associated with lower performance on most neurobehavioural tests after adjusting for multiple comparisons. Although serum acetylcholinesterase was significantly lower in the exposed than the control participants, it was not significantly correlated with either neurobehavioural performance or neurological abnormalities.

Conclusions: Occupational exposure to OP pesticides was associated with deficits in a wider array of neurobehavioural functions than previously reported, perhaps because of higher exposure in this population. Moderate chronic OP exposure may not only affect visuomotor speed as reported previously, but also verbal abstraction, attention, and memory.

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Pesticides are toxic chemicals that are widely used throughout the world. This broad category of compounds includes approximately 600 different active ingredients in use, and a far greater number of commercial products. The main application of pesticides is in agriculture, although its use for public health programmes such as malaria or rodent control is also significant in some areas of the world.[1] Agricultural workers are exposed to pesticides primarily through mixing of chemicals, loading into dispensers, application, clean up, and disposal of empty chemical containers.[2]

Pesticide damage, primarily, the nervous system, and neurobehavioural test methods have been a primary method for detecting this damage in cross sectional workplace research.[3] Surprisingly, there is relatively little neurobehavioural research on workers occupationally exposed to pesticides. Organophosphorous (OP) and carbamate pesticides have been the most intensively studied. Chronic and apparently non-reversing neurobehavioural effects of exposure to OP compounds have been reported, both as sequelae of acute OP poisoning[4–6] and following periods of chronic low level exposure.[7–12]

In Egypt, pesticides are typically applied to cotton crops from May to September (approximately 120 days each year). Approximately 10 000 to 60 000 tons of pesticides are annually used in agriculture or for public health reasons, and 12 000 workers participate in the annual application of pesticides in cotton fields. Safety measures are generally poorly applied, and workers lack proper knowledge or training in safe handling of these chemicals.[13] This may produce a population with higher exposures than described in the other studies reported to date. The purpose of this study was to assess possible neurobehavioural deficits in workers employed for several years to apply OP pesticides to Egypt's cotton crop.

METHODS

Time and setting of the study

This study was conducted in the period from June to September 2000, when pesticides were applied to cotton crops in the field. It was carried out at Menoufiya Governorate, Egypt, where cotton is grown and pesticides are widely used in a large number of fields. A typical workday was from 8 00 am to 12 00 pm, then from 3 00 pm to 7 00 pm, six days per week. The participants were examined during workdays at midday break from about 12 00 pm to 3 00 pm, during which they ate a meal and avoided exposure to the high temperature at that part of the day.

The tests were administered in offices inside buildings of the pesticide application departments (10 buildings in different villages), which belonged to the Egyptian Organisation for Agriculture Credit and Cooperation, Ministry of Agriculture. Sites were selected to conduct examinations and testing in a quiet, comfortable environment with minimal distractions. Each test setting contained office furniture and a table suitable for a clinical examination.

Participants

Pesticide exposed

An official permission letter was obtained from the Ministry of Agriculture to ensure management cooperation. The purpose of the study was explained to the managers and employees at each of the 10 sites. All participants in this study were volunteers who signed a statement of formal consent before testing.

Abbreviations: AchE, acetylcholinesterase; BMI, body mass index; OP, organophosphorous

Table 1 Demographic characteristics of exposed and control participants

Studied variables	Exposed participants (n=52)	Control participants (n=50)	Test of significance	p value
Age (y)				
Mean (SD)	43.63 (5.51)	42.48 (5.54)	1.06*	0.29
Duration of work (y)				
Mean (SD)	18.04 (8.29)	17.08 (4.37)	0.73*	0.47
Degree of education, n (%)				
University	12 (23)	8 (32)	0.81†	0.37
Secondary	40 (77)	42 (68)		
Body mass index (kg/m^2)				
Mean (SD)	27.62 (2.24)	27.89 (2.58)	0.58*	0.57
Smoking, n (%)				
Smokers	18 (34.62)	19 (38.00)	0.13†	0.72
Non-smokers	34 (65.38)	31 (62.00)		
Coffee/tea (cups/day)				
Mean (SD)	5.33 (1.42)	5.02 (1.22)	1.17*	0.25

*Student's *t* test.
†χ^2 test.

The consent form was developed according to the international ethical guidelines for biomedical research involving human subjects prepared by the Council for International Organisations for Medical Sciences in collaboration with the World Health Organisation (Geneva, 1993). The consent form was reviewed and approved by the Ministry of Agriculture, Egypt, which employed and insured the workers recruited into this study. Each participant was asked to do his best on the tests.

Fifty two males were recruited from those who are working in the pesticide application departments at Berket El-Sabe district, Menoufiya Governorate, Egypt (n = 86). Sixty four (74%) employees were eligible for inclusion in the study, while 22 (26%) were ineligible because they were either females or service workers who had never been involved in pesticide application. Among the eligible group, 12 (19%) were excluded or declined to participate, so the overall response rate was 81%. Agriculture engineers constituted 37% of the exposed group. They worked in the fields and were responsible for the entire application procedure, including documentation to register seasonal workers, and types and amounts of pesticides used. Also in the exposed group were assistant agriculture engineers (38%), mixers (10%), and mechanics to repair the spraying devices (15%). The tasks in these job categories required workers to remain in the field throughout the spraying period. Each exposed participant performed these activities virtually every working day, six days per week, during the period between June and September. Table 1 summarises demographic characteristics of the exposed and control participants.

Most participants (88%) reported that they had never used protective clothing; three (6%) of those remaining occasionally, and three (6%) frequently used cloth cone-like masks worn over the nose and mouth to prevent particulate exposure.

All exposed participants had been involved in pesticide application on almost all crops and orchards found in Egypt (including cotton crops). During the past three years they had participated extensively in pesticide applications on cotton crops only. No acute poisoning incidents that led to hospitalisation were reported either during the study or in the past.

Unexposed controls

A control group consisting of 50 male clerks and administrators who had never been exposed to pesticides in their work was recruited from different departments at the Ministry of Agriculture. The response rate among controls invited to participate was 79%. The control participants were from the same socioeconomic class (based on the 1983 criteria of El-Sherbiney and colleagues[14]), lived in the same district, and worked in buildings near the cotton fields where the exposed participants worked. The number of clerks and administrators exceeded the number needed to carry out the work of the department. Therefore, most of them did not spend the entire work time (officially between 8 00 am and 2 00 pm) inside offices. Thus, the time spent by the exposed and control participants working with papers, figures, or numbers was roughly equivalent.

Table 2 Pesticides used for spraying cotton crops in Berket- El-Sabe, Egypt in the period June to September 2000

Types and trade names of used pesticides	Active ingredients
Insect growth regulators	
Cascade	Flufenoxuron
Atabron	Chlorfuazuron
Consult	Hexaflumuron
Bacillus thuringiensis	*Bacillus thuringiensis*
Organophosphorous compounds	
Curacron	Profenofos
Dursban	Chlorpyrifos
Hostathion	Triaziphos
Thimet	Phorate
Carbamates	
Sevin	Carbaryl
Larvin	Thiodicarb
Pyrethroids	
Pyrethroid	Esfenvalerate

Criteria for exclusion

Based on personal data and medical histories, 25 potential exposed and control study participants were excluded because they reported that they were seasonal workers, had less than 12 years of education, or had any of several medical diagnoses (diabetes mellitus, liver or kidney disease, peripheral neuropathy, vitamin deficiency, anaemia, addiction), long term treatment with psychotropic drugs, prior history of head injury resulting in loss of consciousness, or recent exposure to other neurotoxic agents.

Spraying schedule

Based on Egyptian Ministry of Agriculture guidelines, cotton crops were regularly treated with pesticides from the first days of June to the first days of September in 2000. Table 2 lists types and trade names of pesticides used. Typically, pesticides were applied once every 15 days. Insect growth regulators

Table 3 Estimated mean (SEM) neurobehavioural performance for exposed and control participants

Neurobehavioural tests	Control (n=50) Mean (SEM)	Exposed (n=52) Mean (SEM)	Holm adjusted p value*	95% CI for difference†
Verbal abstraction				
Similarities	10.91 (0.23)	9.68 (0.24)	0.003	–1.88 to –0.57
Visuomotor speed				
Digit Symbol	27.19 (0.60)	23.85 (0.62)	0.001	–4.97 to –1.72
Trailmaking A (s)	56.43 (0.90)	60.02 (0.93)	0.030	1.15 to 6.02
Trailmaking B (s)	113.18 (1.56)	119.97 (1.61)	0.015	2.58 to 11.01
Problem solving				
Block design	22.41 (0.61)	20.68 (0.64)	0.124	–3.39 to –0.07
Attention				
PASAT	19.65 (0.16)	19.40 (0.17)	0.568	–0.69 to 0.20
Letter Cancel (errors)	2.83 (0.18)	3.52 (0.19)	0.037	0.19 to 1.18
Memory				
Digit Span Forward	4.87 (0.13)	4.38 (0.13)	0.037	–0.84 to –0.14
Digit Span Backward	3.64 (0.10)	3.09 (0.10)	0.003	–0.84 to –0.28
BVRT	5.48 (0.13)	4.82 (0.13)	0.003	–1.01 to –0.31
Story Recall A	17.93 (0.22)	17.76 (0.22)	0.570	–0.76 to 0.42
Story Recall B	3.09 (0.10)	2.76 (0.10)	0.052	–0.59 to –0.07

Multiple regression was used to adjust for age and education; results are for a 42 year old person with 12 years of education.
*p values less than 0.05 are significant.
†Difference between means; exposed mean – control mean.

were applied in the early stages of cotton growth, then, according to the severity of infestation, either one or a combination of two or three of the OP, carbamate, or pyrethroid insecticides were applied. During this season, ambient temperatures were 30–37ºC and the humidity was typically over 75%. The pesticides were applied by knapsack sprayers (carrying 120 litres of pesticides) or motorised sprayers such as tractors (400–600 litres).

Spraying was carried out by a team of 13–15 persons. This team consisted of 6–7 applicators (seasonal workers who were not included in the study), 5–6 agricultural engineers and assistants, a mixer, and a mechanic. The agriculture engineers, assistants, and seasonal applicators worked closely in the field and their main mode of exposure was by inhalation. Mixers were exposed by both inhalation and skin contact. Mechanics were exposed by inhalation, skin contact, and occasionally ingestion during the repair of old machines.

Tests administered

All participants were subjected to a personal, occupational, and medical history questionnaire. A clinical examination consisting of general, chest, heart, and abdominal examination was administered, along with specific neurological tests for sensory and motor functions including: (1) cranial nerves (for example, sense of smell, visual acuity, visual fields, pupillary reactions, extraocular movements, corneal reflexes, hearing and gag reflex); (2) motor system (for example, involuntary movements, muscle status, muscle tone, muscle power, and coordination); (3) reflexes (for example, knee and ankle reflexes and plantar response); (4) sensory system (superficial sensations—for example, pain and touch sensation; deep sensations—for example, vibration sense; position and discriminate sensations—for example, stereognosis, number identification, and two point discrimination).[15] A series of neurobehavioural tests were also administered: (1) Similarities (test of verbal abstraction); (2) Digit Symbol and Trailmaking part A and B (visuomotor speed); (3) Block Design (problem solving); (4) Paced Auditory Serial Addition Test (PASAT), Letter Cancellation (attention); (5) Digit Span, Benton Visual Retention Test (BVRT), Story Recall parts A and B (memory); and (6) Eysenck Personality Questionnaire (EPQ) (personality).

Better performance is evaluated by higher scores obtained on tests of Similarities, Digit Symbol, Block Design, PASAT, Digit Span, BVRT, and Story Recall tests; by contrast, lower latencies or time to complete Trailmaking part A and B tests and a lower score on the Letter Cancellation test indicated better performance.[16]

A 5 ml sample of venous blood was taken under complete aseptic precautions from 45 of 52 exposed and from 37 of 50 unexposed participants. Seven and 13 of the exposed and control participants, respectively, either refused to give blood or the quantity of blood collected was not sufficient to complete the analysis. Blood samples were sent for analysis of serum acetylcholinesterase (AChE) and liver and kidney function tests.

AChE was measured by HPLC using the colorometric endpoint method according to Rappaport and colleagues[17] (Sigma-Aldrich Corporation, 1997). Liver function (for example, AST, ALT, alkaline phosphatase, serum bilirubin, albumin, globulin, and total proteins) and kidney function (for example, blood urea and serum creatinine) tests were done to exclude participants with any renal or kidney disease who would be at risk of encephalopathy.[15]

Blood samples were collected form all participants after completion of the questionnaire, clinical examination, and neurobehavioural test battery. In the only exception to this, questionnaires were administered to six participants in the fields and blood samples were collected at the same place; clinical examination and the neurobehavioural test battery were carried out later in the same testing room used for other participants.

RESULTS

Demographics

The mean age of the exposed participants (43.63 years) was slightly older than that of controls (42.48 years), but the difference was not significant (p = 0.29) (see table 1). The mean duration of Ministry of Agriculture employment of the exposed participants was 18.04 years, and the mean of the control group was 17.08 years. This difference was also not significant (p = 0.47). Most of the exposed and control participants had completed secondary school education (77% and 68%, respectively), while the remainder had completed university education (23% and 32%, respectively). The difference was not significant (p = 0.37).

Measures reflecting lifestyle choices did not differ between the groups. Body mass index (BMI) was measured because OP pesticides have been reported to reduce food intake,[18] and the

Table 4 Regression analysis of neurobehavioural performance by duration of exposure adjusted for age and education

Neurobehavioural tests	β (SE)*	Holm adjusted p value	95% CI†
Verbal abstraction			
Similarities	−0.66 (0.15)	<0.001	−0.96 to −0.36
Visuomotor speed			
Digit Symbol	−1.82 (0.41)	<0.001	−2.64 to −1.01
Trailmaking A (s)	2.40 (0.60)	0.001	1.21 to 3.60
Trailmaking B (s)	4.24 (1.08)	0.001	2.10 to 6.38
Problem solving			
Block Design	−0.82 (0.43)	0.178	−1.67 to 0.02
Attention			
PASAT	−0.04 (0.12)	1.000	−0.27 to 0.19
Letter Cancel	0.32 (0.13)	0.078	0.07 to 0.57
Memory			
Digit Span Forward	−0.32 (0.09)	0.004	−0.50 to −0.14
Digit Span Backward	−0.28 (0.07)	<0.001	−0.41 to −0.15
BVRT	−0.28 (0.09)	0.004	−0.46 to −1.00
Story Recall A	−0.08 (0.15)	1.000	−0.39 to 0.22
Story Recall B	−0.15 (0.07)	0.138	−0.28 to −0.002

*β = regression coefficient computed for each decade.
†CI, confidence interval.

Table 5 Mean (SD) Eysenck Personality Assessment Questionnaire (EPQ) in exposed and control participants

Personality assessment	Exposed (n=52) Mean (SD)	Control (n=50) Mean (SD)	*t* test	p value
Psychoticism	3.42 (0.89)	3.40 (0.99)	0.12	0.90
Neuroticism	9.90 (1.16)	9.24 (1.61)	2.67	0.01
Extraversion	13.06 (1.89)	12.76 (1.66)	0.84	0.40
Criminality	9.73 (1.71)	9.64 (1.59)	0.28	0.78
Lie scale	8.02 (1.52)	8.40 (1.39)	1.32	0.19

concentration of certain pesticides may remain higher in obese people for a longer time.[19 20] However, the mean BMI of the exposed and control participants was virtually the same ($p = 0.57$). Self report of smoking habits of the two groups was not significantly different, none of the participants reported a history of drinking alcohol, and the mean number of cups of tea and/or coffee consumed per day was virtually the same in both groups (table 1).

The mean level of serum AChE, an indicator of exposure to OP pesticides, was significantly lower in the exposed (87.34 U/ml) than in control (108.25 U/ml) participants ($p = 0.0001$). Multiple regression analysis showed that serum AChE was significantly associated with exposure ($\beta = -21.34$, SE 3.94, 95% CI −29.18 to −13.50), while age, education, and BMI had no significant effect on AChE ($F = 0.73$, df = 3, 77, $p > 0.05$).

Neurobehavioural performance

Exposed workers exhibited lower performance than controls on most of the neurobehavioural tests (table 3). Although the groups did not differ significantly with respect to age and education, these variables are so well established as confounders of neurobehavioural performance,[16 21] that multiple linear regression analysis was used to adjust for their influence (with the midpoints of each category as the independent variable). Holm's modification of the Bonferroni correction equation was applied to adjust for multiple comparisons.[22] After adjustment for confounders and multiplicity, performance of the exposed participants was significantly lower on Similarities, Digit Symbol, Trailmaking part A and B, Letter Cancel, Digit Span Forward and Backward, and Benton Visual Retention (table 3).

Effects of serum AChE and duration of work in pesticide application departments on neurobehavioural performance were tested using regression analysis models. Age and education were used in the models as covariates to eliminate their impact, as these factors also co-vary with duration of exposure. Serum AChE did not show any significant effect on performance of the exposed workers. In contrast, there was a trend towards lower performance scores as duration of exposure increased; the difference was significant on Similarities, Digit Symbol, Trailmaking part A and B, Digit Span Forward and Backward, and Benton Visual Retention (table 4). Negative association was reported on the Similarities, Digit Symbol, Digit Span Forward and Backward, and BVRT tests, all of which measured the number of items completed in a fixed time (that is, higher scores reflect better performance). Conversely, there was a significant positive association with Trailmaking part A and B, in which time to completion was the primary measure (that is, lower scores reflect better performance).

Personality and clinical assessment

The Eysenck personality questionnaire revealed that the mean neuroticism score of the exposed participants was significantly higher than that of the controls ($p = 0.01$), while psychoticism, extraversion, and criminality showed no significant differences between the exposed and control participants (table 5).

Symptoms of dizziness and numbness were significantly higher in the exposed than the control group. While other symptoms and signs were higher in the exposed participants, they were not significant (table 6). Most of the reported neurological symptoms and signs were significantly higher in older workers who, of course, also had the longest work duration, compared to those who were younger and had a shorter

Table 6 Prevalence (%) and odds ratios of symptoms and signs in exposed and control participants

Neurological symptoms† and signs‡	Exposed (n=52) n (%)	Control (n=50) n (%)	OR	95% CI	Holm adjusted p value*
Blurred vision	15 (29)	5 (10)	3.64	1.28 to 12.07	0.102
Dizziness	14 (27)	2 (4)	8.84	22.29 to 58.52	0.008
Numbness	13 (25)	1 (2)	16.33	3.05 to 303	0.003
Headache	15 (29)	11 (22)	1.44	0.59 to 3.60	0.489
Tremors	8 (15)	1 (2)	8.91	1.55 to 169	0.101
Fatigue	15 (29)	6 (12)	2.97	1.09 to 9.05	0.197
Muscle power	5 (10)	1 (2)	5.21	0.80 to 102	0.281
Ankle reflex	6 (12)	1 (2)	6.39	1.04 to 123	0.225
Knee reflex	9 (17)	3 (6)	3.28	0.91 to 15.50	0.281
Superficial sensation	12 (23)	3 (6)	4.70	1.38 to 21.69	0.101
Deep sensation	1 (2)	0 (0)	–	–	0.489

*Significant after using Holm's modification of Bonferroni correction (6 symptoms and 5 signs).
†Have you ever had a history of any of the following symptoms?
‡Detected by clinical examination.
OR, odds ratio; CI, confidence interval.

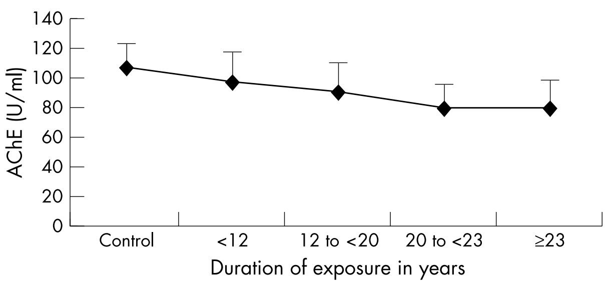

Figure 1 Relation of mean (SD) AChE (U/ml) and years of exposure to pesticides.

duration of work. Serum AChE showed no significant differences ($p > 0.05$) between those with positive or negative neurological symptoms or signs, although there was a significant trend of lower AChE levels as exposure duration increased ($\beta = -1.18$, SE 0.19, 95% CI −1.55 to −0.81 (fig 1).

DISCUSSION

The exposed participants showed a consistent, statistically significant pattern of lower neurobehavioural functioning compared to controls, after adjustment for multiple comparisons.[22] This pattern was supported by multiple regression analysis, which adjusted for age and education, the strongest contributors to neurobehavioural performance.[16 21] The deficits were seen in a wide array of neurobehavioural functions, including verbal abstraction (Similarities), visuomotor speed (Digit Symbol and Trailmaking part A and B), visual attention (Letter Cancellation), auditory attention and memory (Digit Span), and visual memory (BVRT) (table 3).

Additional analyses supported the association of the neurobehavioural deficits with work in agriculture. Duration of work in agriculture was inversely correlated with neurobehavioural performance (table 4). The longer the period of agricultural work, and thus exposure to pesticides, the greater the performance deficits of the exposed participants relative to controls. By contrast, there was no evidence that the performance was affected by current OP pesticide exposure. All serum AChE values were within normal limits (40–120 U/ml according to the 1997 Sigma-Aldrich Corporation manual), suggesting that participants were free from acute OP effects at the time of testing. Also, most of the neurological symptoms and signs were markedly prominent among older age participants and among participants with more years of exposure. This is in

Table 7 Comparison of neurobehavioural tests in primary studies of occupational long term exposure to OP pesticides and non-reversing sequelae to OP poisoning

	Occupational long term exposure			Non-reversing sequelae of OP poisoning		
Neurobehavioural tests	Present study (2001) (n=52)	Stephens *et al* (1995) (n=146)	Korsak and Sato (1977) (n=32)	Steenland *et al* (1994) (n=128)	Rosenstock *et al* (1991) (n=36)	Savage *et al* (1988) (n=100)
Verbal abstraction						
Similarities	⇓*	nd	nd	nd	nd	⇓*
Visuomotor speed						
Digit Symbol	⇓*	⇓*	nd	⇓*	⇓*	⇓*
Trailmaking B	⇓*	nd	⇓*	nd	nd	⇓*
Trailmaking A	⇓*	nd	nd	nd	⇓*	nd
Problem solving						
Block Design	⇓*	nd	nd	nd	⇓*	⇓
Attention						
PASAT	⇓	nd	nd	nd	nd	nd
Letter Cancel	⇓*	nd	nd	nd	nd	nd
Memory						
Digit Span	⇓*	nd	nd	nd	⇓*	⇓*
BVRT	⇓*	nd	nd	nd	⇓*	nd
Story Recall A	⇓	nd	nd	nd	nd	nd
Story Recall B	⇓	nd	nd	nd	nd	nd

⇓=worse performance.
*p<0.05.
nd, no data; test not administered.

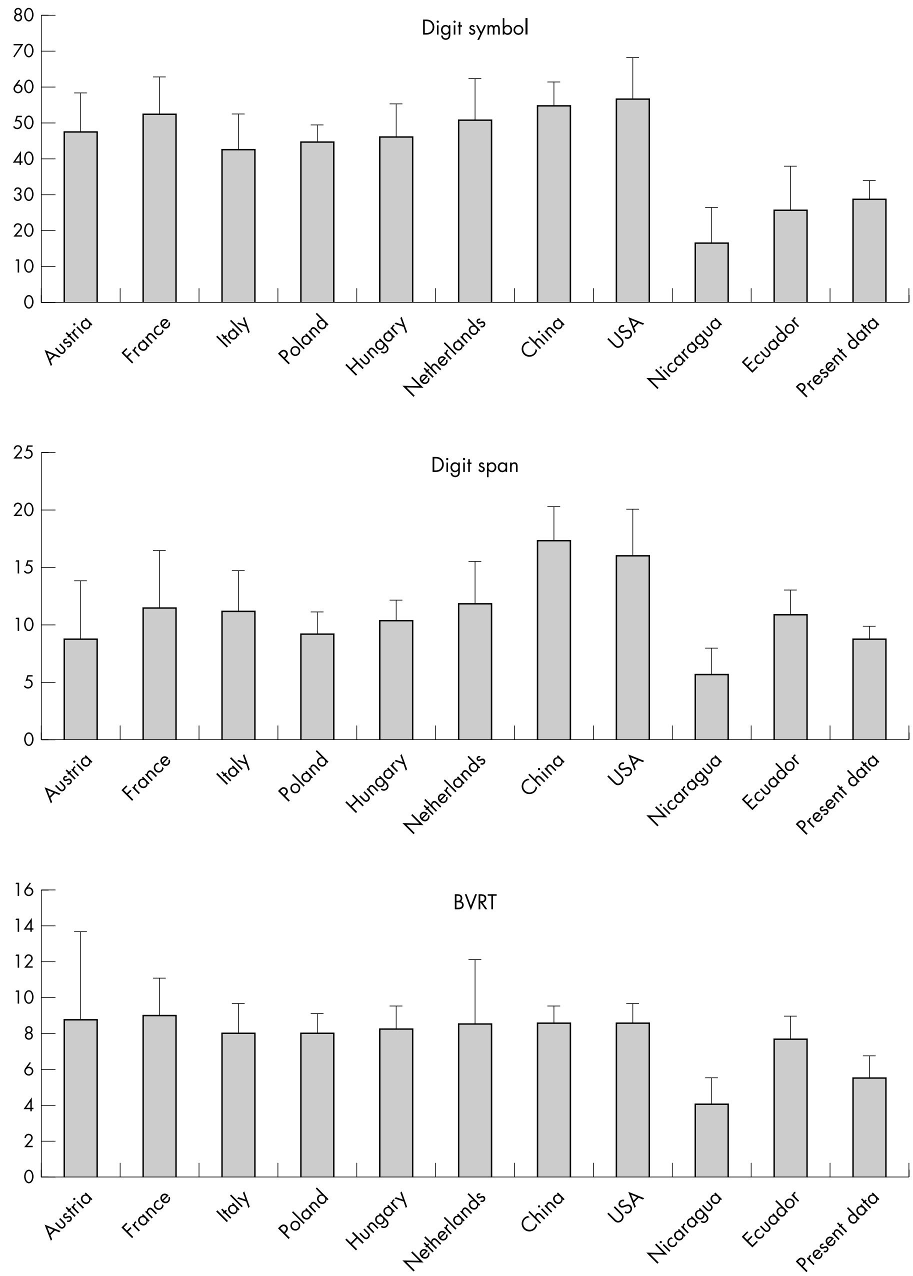

Figure 2 Performance of unexposed control from different countries[24 25] compared to controls in the present study.

accordance with Davignon and colleagues[23] and Amr and colleagues[24] who reported that annual exposure to pesticides over a period of 10–20 years can result in mild to severe deterioration in neurological function.

Comparison with previous research

The reported neurobehavioural deficits in chronically exposed workers can be compared to other studies of both chronically exposed and acutely poisoned individuals (table 7). In two studies of chronically exposed sheep farmers in the UK, farmers performed significantly worse than controls (non-exposed quarry workers) on tests measuring sustained attention and speed of information processing, including the Digit Symbol test.[11] Savage and colleagues,[4] Rosenstock and colleagues,[5] and Steenland and colleagues[6] examined the possible non-reversing effects in people who have been poisoned or seen by a physician following overexposure to OP compounds. Each study has limitations, but together they reveal consistent differences in these populations, a pattern of deficits that is increasingly credible because of the consistency of the findings among the studies. These consistent findings of deficits are seen on the Digit Symbol, Trailmaking, Block Design, Digit Span, and Benton Visual Retention tests (table 7). The findings in the present study parallel those in Stephens and colleagues[11] and other studies of OP exposures, but suggest that the neurobehavioural functions affected are far broader than previously reported (table 7, column 2).

The scores on the tests in this study are lower when compared to scores reported in many other countries.[25–27] Figure 2 presents data from unexposed controls in these studies. A major concern when performance is low is that control performance may be so near the performance "floor" that true pesticide related differences could not be detected. However, in the present study, while dramatic clinical differences were not seen between exposed and control participants (for example, table 6), many test differences were significant, even after adjustment for multiple comparisons (table 3). The lower scores may arguably be attributed to differences in the educational background and the general inexperience with the testing situation in some countries.[26 27] The participants in the present study were encouraged to apply themselves to the tests and were observed to work diligently on the tests, supporting the validity of the results.

Personality measures

Regarding the assessment of personality, the Lie scale (L) score was not significantly different between exposed (mean 8.02 (SD 1.52)) and control (8.40 (1.39)) participants ($p = 0.19$). This lack of difference supports the accuracy of the results of the other scales. Further, the Lie scale is designed to indicate the extent to which the individual is being honest or trying to create a false impression (faking bad),[28 29] and thus also supports the validity of the neurobehavioural test performance scores. This study revealed that the mean (SD) neuroticism score of the exposed participants (9.98 (1.16)) was significantly higher than that of the controls (9.24 (1.61)) ($p = 0.01$), while psychoticism, extraversion, and criminality showed no significant group differences ($p > 0.01$) (table 5). Neuroticism is the name Eysenck[28 29] gave to a dimension that ranges from normal, fairly calm and collected people to those who tend to be quite "nervous". Other investigators have also reported psychiatric disorders, particularly neurosis, anxiety, obsessive-compulsive behaviour, phobias, temper outbursts, irritability, and depression in OP exposed participants.[11 12 25 30–34]

Acetylcholinesterase measure

Serum acetylcholinesterase was significantly lower in the exposed than the control participants ($\beta = -21.34$, SE 3.94, 95% CI −29.18 to −13.50). As Namba and colleagues[34] noted, OP pesticides do not accumulate in tissue. However, a cumulative effect is produced in the form of reduction of AChE and other tissue esterases since these enzymes serve as buffers, protecting AChE of the synapse.[35] This reduction may be related to the phenomenon of aging of AChE as a result of long term enzyme inhibition,[36] as supported by the significant negative correlation between AChE and duration of exposure in the present study (fig 1). Clinical experience with workers exposed to OP compounds reveals that some may exhibit mild symptoms of intoxication without any significant change in blood AChE activity.[37–39] It has been suggested that AChE is insensitive to subtle, subclinical alternations in motor and cognitive functions, possibly related to the low level OP exposure.[39]

Broader range of OP effects suggested

The neurological symptoms of dizziness and numbness were significantly more prevalent in exposed than control workers in the present study (OR = 6.75 and 12.5, respectively, table 6). Odds ratios in table 6 are computed from a logistic regression model. Confidence intervals for odds ratio are based on the likelihood ratio test and are known to be more accurate for small sample sizes.[40] Amr[41] reported that blurred vision, dizziness, numbness, paraesthesia, headache, vertigo, asthenia, superficial sensory loss, trophic and vasomotor changes, and decreased ankle and deep reflexes were more prevalent among Egyptian pesticide applicators than controls. These findings may suggest that these groups of Egyptian cotton pesticide applicators have sustained higher exposures than seen in the other studies noted here.[9 11 12] The symptoms of dizziness and numbness may suggest the beginning of nervous system effects that could be on the verge of becoming clinically detectable. This may explain why the exposed participants in this study had deficits on so many more neurobehavioural tests than in the other studies of pesticide exposed workers. If this is true, the effects of low to moderate level chronic OP exposure may be more wide ranging than previously realised. Chronic OP exposure has been associated with visuomotor speed as indicated by the Digit Symbol and Trailmaking B tests.[9 11] The results of the present study confirm these findings. However, the present study also suggests that moderate exposure to OP compounds over several years for approximately 120 days per year, may also be associated with deficits on verbal abstraction, attention, and memory. The implication of these findings may be considerable, especially in the developing world, where poisoning is increasingly common and where economic, climatic, social, and cultural conditions are likely to thwart the implementation of preventive approaches to poisoning that have been successfully used in industrialised nations.[42 43]

Main messages

- Occupational exposure to OP pesticides is associated with deficits in a wider array of neurobehavioural functions than previously reported, perhaps because of higher exposure in the studied population.
- Moderate chronic OP exposure may not only affect visuomotor speed as reported previously, but also verbal abstraction, attention, and memory.
- Assessment of neurobehavioural deficits is a useful method for early detection of chronic effects of OP pesticide exposure.

Policy implications

- The implications of the present findings may be considerable, especially in developing countries where poisoning is increasingly common, and economic, climatic, social, and cultural conditions are likely to thwart the implementation of preventive approaches.
- An immediate priority in developing countries is to nurture the human resources required to develop and sustain training strategy, using low cost and more effective training interventions.

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